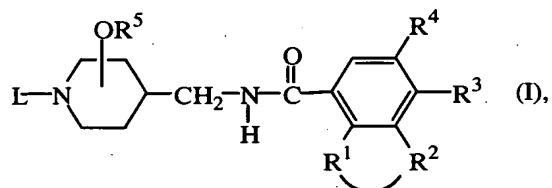


## Claims

### 1. A compound of formula (I)



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a stereochemically isomeric form thereof, an *N*-oxide form thereof, or a pharmaceutically acceptable acid or base addition salt thereof, wherein -R<sup>1</sup>-R<sup>2</sup>- is a bivalent radical of formula

10	-O-CH <sub>2</sub> -O-	(a-1),
	-O-CH <sub>2</sub> -CH <sub>2</sub> -	(a-2),
	-O-CH <sub>2</sub> -CH <sub>2</sub> -O-	(a-3),
	-O-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -	(a-4),
	-O-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -O-	(a-5),
15	-O-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -	(a-6),
	-O-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -O-	(a-7),
	-O-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -	(a-8),

wherein in said bivalent radicals optionally one or two hydrogen atoms on the same or a different carbon atom may be replaced by  $C_{1-6}$ alkyl or hydroxy,

20         $R^3$  is  $C_{1-6}$ alkyl,  $C_{1-6}$ alkyloxy, or halo;

$R^4$  is hydrogen or halo;

provided that when  $R^3$  and  $R^4$  are both halo, then the bivalent radical- $R^1-R^2-$  is of formula (a-5);

$R^5$  is hydrogen or  $C_{1-6}$ alkyl, and the  $-OR^5$  radical is situated at the 3- or 4-position of the piperidine moiety;

L is hydrogen, or L is a radical of formula

- Alk-R<sup>6</sup> (b-1),
- Alk-X-R<sup>7</sup> (b-2),
- Alk-Y-C(=O)-R<sup>9</sup> (b-3), or
- Alk-Z-C(=O)-NR<sup>11</sup>R<sup>12</sup> (b-4).

wherein each Alk is C<sub>1-12</sub>alkanediyi; and

R<sup>6</sup> is hydrogen; hydroxy; cyano; C<sub>3-6</sub>cycloalkyl; C<sub>1-6</sub>alkylsulfonylamino; aryl or Het;

$R^7$  is  $C_{1-6}$ alkyl;  $C_{1-6}$ alkyl substituted with hydroxy;  $C_{3-6}$ cycloalkyl; aryl or Het;

X is O, S, SO<sub>2</sub> or NR<sup>8</sup>; said R<sup>8</sup> being hydrogen or C<sub>1-6</sub>alkyl;  
R<sup>9</sup> is hydrogen, C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy or aryl;  
Y is a direct bond, or NR<sup>10</sup> wherein R<sup>10</sup> is hydrogen or C<sub>1-6</sub>alkyl;  
Z is a direct bond, O, S, or NR<sup>10</sup> wherein R<sup>10</sup> is hydrogen or C<sub>1-6</sub>alkyl;  
5 R<sup>11</sup> and R<sup>12</sup> each independently are hydrogen, C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, or R<sup>11</sup> and R<sup>12</sup> combined with the nitrogen atom bearing R<sup>11</sup> and R<sup>12</sup> may form a pyrrolidinyl, piperidinyl, piperazinyl or 4-morpholinyl ring both being optionally substituted with C<sub>1-6</sub>alkyl;  
aryl represents unsubstituted phenyl or phenyl substituted with 1, 2 or 3 substituents  
10 each independently selected from halo, hydroxy, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkylcarbonyl, nitro, trifluoromethyl, amino, aminocarbonyl, and aminosulfonyl; and  
Het is furanyl; furanyl substituted with C<sub>1-6</sub>alkyl or halo;  
tetrahydrofuranyl; tetrahydrofuranyl substituted with C<sub>1-6</sub>alkyl;  
15 dioxolanyl; dioxolanyl substituted with C<sub>1-6</sub>alkyl;  
dioxanyl; dioxanyl substituted with C<sub>1-6</sub>alkyl;  
tetrahydropyranyl; tetrahydropyranyl substituted with C<sub>1-6</sub>alkyl;  
2,3-dihydro-2-oxo-1H-imidazolyl; 2,3-dihydro-2-oxo-1H-imidazolyl  
20 substituted with one or two substituents each independently selected from halo, or C<sub>1-6</sub>alkyl;  
pyrrolidinyl; pyrrolidinyl substituted with one or two substituents each independently selected from halo, hydroxy, or C<sub>1-6</sub>alkyl;  
pyridinyl; pyridinyl substituted with one or two substituents each independently selected from halo, hydroxy, C<sub>1-6</sub>alkyl;  
25 pyrimidinyl; pyrimidinyl substituted with one or two substituents each independently selected from halo, hydroxy, or C<sub>1-6</sub>alkyl;  
pyridazinyl; pyridazinyl substituted with one or two substituents each independently selected from hydroxy, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkyl or halo;  
pyrazinyl; pyrazinyl substituted with one or two substituents each  
30 independently selected from hydroxy, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkyl or halo.

2. A compound as claimed in claim 1 wherein the -OR<sup>5</sup> radical is situated at the 3-position of the piperidine moiety having the trans configuration.
- 35 3. A compound as claimed in claim 2 wherein the absolute configuration of said piperidine moiety is (3S, 4S).

4. A compound as claimed in any of claims 1 to 3 wherein -R<sup>1</sup>-R<sup>2</sup>- is a radical of formula (a-5), R<sup>3</sup> is chloro and R<sup>4</sup> is chloro.

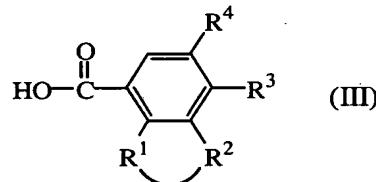
5. A compound as claimed in any of claims 1 to 3 wherein -R<sup>1</sup>-R<sup>2</sup>- is a radical of formula (a-5), R<sup>3</sup> is chloro and R<sup>4</sup> is bromo.

6. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically active amount of a compound according to any of claims 1 to 5.

10 7. A process for preparing a pharmaceutical composition according to claim 6 wherein a therapeutically active amount of a compound according to any of claims 1 to 5 is intimately mixed with a pharmaceutically acceptable carrier.

15 8. A compound according to any of claims 1 to 5 for use as a medicine.

9. A compound of formula (III)



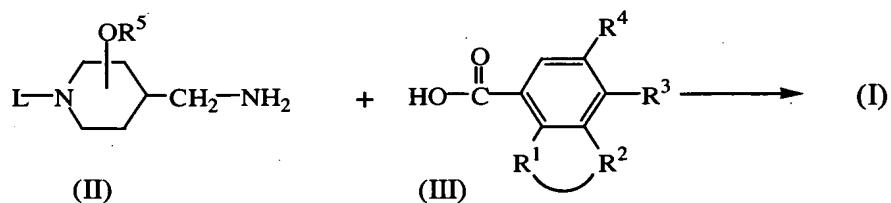
wherein

20 -R<sup>1</sup>-R<sup>2</sup>- is a bivalent radical of formula  

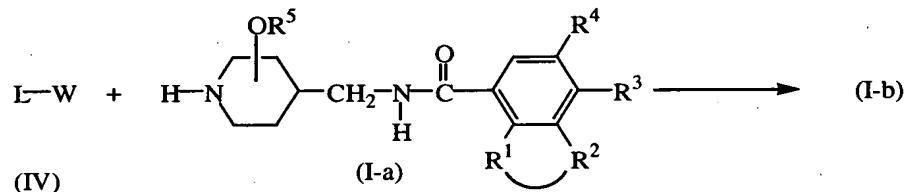
$$-\text{O}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{O}- \quad (\text{a-5}),$$
  
 wherein in said bivalent radicals optionally one or two hydrogen atoms on the same  
 or a different carbon atom may be replaced by C<sub>1-6</sub>alkyl or hydroxy;  
 R<sup>3</sup> is C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, or halo; and  
 25 R<sup>4</sup> is hydrogen or halo.

10. A process for preparing a compound of formula (I) wherein

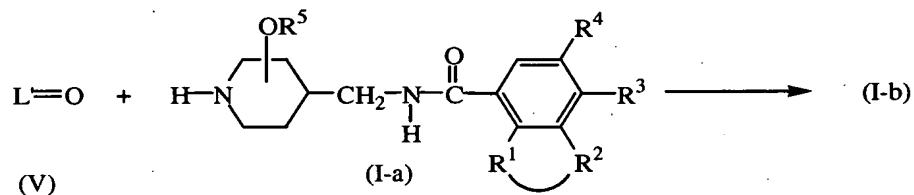
a) an intermediate of formula (II) is reacted with an carboxylic acid derivative of formula (III) or a reactive functional derivative thereof;



b) an intermediate of formula (IV) is *N*-alkylated with a compound of formula (I-a), defined as a compound of formula (I) wherein L represents hydrogen, in a reaction-inert solvent and, optionally in the presence of a suitable base, thereby yielding compounds of formula (I-b), defined as compounds of formula (I) wherein L is other than hydrogen;



10 c) an appropriate ketone or aldehyde intermediate of formula  $L'=O$  (V), said  $L'=O$  being a compound of formula  $L-H$ , wherein two geminal hydrogen atoms in the  $C_{1-12}$ alkanediyl moiety are replaced by  $=O$ , is reacted with a compound of formula (I-a), thereby yielding compounds of formula (I-b);



15 wherein in the above reaction schemes the radicals -R<sup>1</sup>-R<sup>2</sup>-, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are as defined in claim 1 and W is an appropriate leaving group;

20 d) or, compounds of formula (I) are converted into each other following art-known transformation reactions; or if desired; a compound of formula (I) is converted into a pharmaceutically acceptable acid addition salt, or conversely, an acid addition salt of a compound of formula (I) is converted into a free base form with alkali; and, if desired, preparing stereochemically isomeric forms thereof.